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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/992,149	11/06/2001	Robert George Brown	84077	5280

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EXAMINER	
MINNIFIELD, NITA M	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 03/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/992,149	BROWN ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed November 28, 2003 is acknowledged and has been entered. Claims 16-43 have been canceled. Claims 1, 5-7, 9, 10, 12 and 14 have been amended. Claims 1-15 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment and/or comments with the exception of those discussed below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The Brown/Kimmins/Pohajdak Declaration filed on November 28, 2003 under 37 CFR 1.131 is sufficient to overcome the 102 (a) Brown et al WO 00/37100 reference.

4. Claims 5, 6 and 14 are objected to because of the following informalities: these claims contain trademark items. Appropriate correction is required.

This objection is maintained as the claims still recite a Trademark item.

5. Claims 5, 6, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are vague and indefinite in the recitation of trademark items "TiterMax™" and "Phospholipon 90 G™". The metes and bounds of these items are not known and it is not known if

the composition of these items will remain the same in the future. All claim language and limitations should be clearly defined.

6. The Examiner acknowledges the 1.132 Declaration of Brown filed November 28, 2003; however it is not clear why this Declaration was submitted. The previous Office Action did not contain any 112, first paragraph enablement rejections.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nash et al 1985 (J. Reprod. Immunol., 7:151-162) or Alving et al (6110492) taken with Glenn et al (5980898), Gupta et al (Vaccine, 1993, 11/13:293-306) and Edelman et al (Intern. Rev. Immunol., 1990, 7/1:51-66).

The claims are directed to vaccine compositions comprising a carrier comprising a continuous phase of a hydrophobic substance (oil or emulsion), liposomes (cholesterol and a phospholipid), antigen and adjuvant (alum, aluminum or TiterMax), wherein the antigen is encapsulated in said liposomes, and the antigen, which when not in said vaccine composition has a conformation other than its native conformation with the proviso that said antigen is other than a zona pellucida-derived antigen.

Nash et al teaches a composition comprising an antigen (hCG), a water-in-oil emulsion (i.e. carrier), aluminum hydroxide (i.e. adjuvant) and a liposome (see abstract; materials and methods, pp. 152-153). The composition is administered to rabbits (p. 153). The antigen, hCG, is a mammalian antigen. The antigen is other

than the zona pellucida-derived antigen. Alving et al teaches a composition comprising an emulsion (i.e. carrier), antigen and adjuvant (see abstract; examples; claims). The composition also comprises liposomes (cols. 3, 5). The antigen can be prostate-specific antigen, a mammalian antigen (col. 7) and the adjuvant is alum for example (col. 7). The prior art discloses the claimed invention except for the antigen being encapsulated in the liposomes.

However, Glenn et al teaches a formulation comprised of antigen and adjuvant (cols. 2-3). Glenn et al teaches that in addition to the antigen and adjuvant the formulation may comprise a hydrating agent such as a liposome and water-in-oil emulsions or oil (i.e. carrier comprising a continuous phase of a hydrophobic substance) (col. 3, l. 55-63). Glenn et al teaches that the antigen may be derived from a bacterium, virus, fungus, parasite, tumor cell, normal cell, or tumor antigen (cols. 3-4; col. 9). The antigen may be obtained by recombinant means, chemical synthesis, or purification from a natural source (col. 4, l. 7-12; col. 8, l. 12-18; col. 8, l. 44). Glenn et al teaches that the antigen can be incorporated directly into a liposome (col. 8, l. 63-64). Glenn et al teaches that the antigen can be an antigen from hepatitis serotypes A to E (i.e. hepatitis B antigen) (col. 9, l. 13-24). Glenn et al teaches that the adjuvant can be a derivative of lipid A (col. 9). Glenn et al teaches that the antigen can be encapsulated in the liposome (col. 12).

Further, Gupta et al teaches that liposomes act as a vehicle for the antigens. "Not only is the clearance of antigens incorporated into liposomes markedly prolonged but the liposomes may also ensure that a certain amount of antigen is made available for a single antigen-presenting cell at a time following phagocytosis of the liposomes. There are suggestions that liposomes increase

antigen presentation to macrophages. The cell-mediated immunity is believed to be stimulated due to the hydrophobic nature of liposomes. As mentioned earlier, adjuvants like LPS, lipid A or MDP when incorporated into liposomes along with recombinant antigen of *Plasmodium falciparum* and mixed with alum, stimulated a high antibody response to the antigen with no pyrogenicity or toxicity in humans." (p. 299). Gupta et al also teaches that "[o]ral administration of antigen in liposomes resulted in an augmented mucosal response compared with the response obtained with oral antigen alone." (p. 299). Edelman et al teaches various types of adjuvants (see Table 1, p. 52). Edelman et al teaches that more than 16 antigens in liposomes have been published and show an enhanced vaccine (p. 59).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the components as taught in Nash et al and Glenn et al or Alving et al and Glenn et al to make a composition comprising a carrier (i.e. water-in-oil emulsion or oil) a liposome, an antigen encapsulated in liposome and an adjuvant. Glenn et al, Gupta et al, as well as Edelman et al all teach the use of various antigens as well as the encapsulation of those antigens in the liposome. Gupta et al teaches that the immune response was better if the antigen were encapsulated in the liposome (see p. 299); therefore it would have been obvious to a person of ordinary skill in the art to encapsulate the antigen in the liposome to increase the immune response or vaccine protection of the composition. It is noted that even though Applicants recites different names for some of the composition components (see claim 1 (a) carrier, (b) liposome, (d) adjuvant) the composition essentially consists of several adjuvants and an antigen. The prior art references teach that more than one adjuvant can be used in a composition, see for example Nash et al or Alving et al. It is noted that the

recitation of "vaccine" is viewed as intended use. The recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). The claimed invention is prima facie obvious in view of the combine teaches absent any convincing evidence to the contrary.

11. No claims are allowed.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will

be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM

February 23, 2004